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THE EFFECT OF EXPERIMENTAL HYPERTHYROIDISM ON GASTRO-INTESTINAL MOTILITY

A PART OF A DISSERTATION SUBMITTED TO THE GRADUATE FACULTY IN CANDIDACY FOR THE DEGREE OF DOCTOR OF PHILOSOPHY

DEPARTMENT OF PHYSIOLOGY

By
DOROTHY FETTER

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I. THE EFFECT OF EXPERIMENTAL HYPERTHYROIDISM ON GASTRO-INTESTINAL MOTILITY[1]

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From the Physiological Laboratory of the University of Chicago

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Hyperthyroidism as it is observed in the clinic is frequently accompanied by gastro-intestinal symptoms, the most common of which are increased desire for food, and diarrhea. Since in hyperthyroidism oxidation is increased, more food is necessary than normal in order that the tissues of the body should not be used. A hyperthyroid patient may require a diet containing as many as 5,000 calories in order to maintain his body weight (1). Exercise of any kind is accomplished with a greater expenditure of calories than normal. Therefore it may be assumed that the increased desire for food is an adjustment to a new bodily demand, and is a generalized sensation. Carlson has shown that hunger is a sensation accompanying movements of the empty stomach (2); in conditions where hunger is abnormally keen, contractions of the stomach are increased in height and frequency (3). Presumably then the increased desire for food in hyperthyroid patients may be related to an increased motor activity of the empty stomach. Perussé and Rozen (4) have studied the activity of the empty stomach of dogs during periods of feeding with desiccated thyroid, and found that the motility varied, depending upon the amount of thyroid administered. Kratinoff (5) has also studied the effects of induced hyperthyroidism upon the activity of the stomach and duodenum of dogs, and found in some cases an elevation, and in some cases a depression of the motility.

The diarrhea of hyperthyroidism also indicates an increased motility of the digestive tract. King (6) mentions diarrhea as one of the most frequent and annoying symptoms of the disease. He attributes it to the lack of free hydrochloric acid which allows the pylorus to stay open and food to pass on before digestion has occurred, thereby giving greater stimulation to the intestinal tract. Eppinger and Hess (7) attribute the diarrhea to the increased activity of the vagus nerve. Crotti (8) says that the stomach of goiter patients is in a state of constant spasticity as observed fluoroscopically. Baker (9) mentions diarrhea as a common

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symptom in exophthalmic goiter. Lockwood (10) finds diarrhea present in only 4.4 per cent of the 90 cases with an average basal metabolic rate of +35 which he studied. Urmössey and Lukacs (11) found that in 15 of 24 cases gastro-intestinal motility of babies was speeded up by treatment with thyroid material. Deusch (12) also finds that thyroglandal injections increase intestinal motility as revealed by the fluoroscope.

Our work includes studies of the effect of thyroid feeding on the motor activity of the gastro-intestinal tract of dogs. We studied the effect of thyroid feeding on the gastric contractions of the empty stomach, and also on the movement of food through the digestive canal.

Methods. The experiments to be described were run on six dogs. The dogs were kept on a constant diet consisting of 250 grams of meat, 250 cc. of milk, and 200 grams of bread per day. On this diet the dogs maintained their normal weight. The general condition of the dogs was watched, and the weight and temperature were recorded every other day. On one dog basal metabolism tests were frequently taken.

The activity of the gastro-intestinal tract was studied when the stomach was empty by means of the balloon method. The dogs were trained to swallow a stomach tube with a condom balloon attached and the records of the contractions of the empty stomach were taken according to the method suggested by Boldyreff and perfected by Carlson. A bromoform monometer was used, and the pressure at the beginning of each experiment was one centimeter of bromoform. The motility was recorded for a period of three hours, beginning 20 or 24 hours after the dogs had been fed.

The progress of food through the digestive tract was observed by means of the fluoroscope. Once a week, instead of the usual meal, the dogs were fed 200 grams of ground meat mixed with 70 grams of barium sulphate. Note was taken 1, of the time when food first left the stomach; 2, of the time when material entered the ascending colon; 3, of the emptying time of the stomach; 4, of the emptying time of the colon.

The gastric motility was studied by the above methods on the normal dogs for a period varying from two weeks to one month. The dogs were then fed daily 0.4 gram per kilo body weight of Armour's desiccated thyroid in addition to the usual meal. On this amount of thyroid the body temperature rose and the weight decreased. The dog on whom basal metabolism studies were made showed a basal rate increased to +50 per cent. The dogs showed increased nervousness, if restlessness, irritability of temper, and twitchings of the muscles are indications of this condition. Although the water balance was not measured, it was obvious that the dogs drank far more water than normally and urinated more copiously. All the dogs showed an increased desire for food; three showed diarrhea (13). By means of these symptoms it can be seen that the condition in dogs during the feeding of thyroid material resembles spontaneous hyperthy-

roidism in man. The hunger contractions and the progress of the barium meal were studied throughout the period of thyroid feeding. This period varied from one to two months depending on the time necessary for the symptoms to manifest themselves, and their severity.

After thyroid feeding was discontinued, the gastro-intestinal activity was studied for a period of from one to two months.

Results. 1. *Gastric contractions.* In our six dogs, the normal type of gastric contractions varied. Three of these dogs showed low motility, described by Carlson as the 20 second rhythm (14), type 1, or complete rest of the stomach. On the remaining three dogs vigorous type 2 contractions (15) were usually observed.

The gastric motility of all dogs definitely increased over the normal during the period of induced hyperthyroidism. Records of higher activity were obtained about a week after the ingestion of thyroid was initiated. The length of the hunger periods and the height of the individual contractions were increased, also periods of increased tonus became frequent. A vigorous type of activity showing type 2 contractions on which were superimposed smaller contractions of the 20 second rhythm was observed frequently in all dogs during the "hyperthyroid" period.

After the thyroid feeding was discontinued, gastric motility remained high for a few days (average, six) and thereafter dropped. In two dogs the motility steadily decreased to the normal level and remained there. In the other dogs, while the motility decreased below that observed in the hyperthyroid phase, it did not drop to the normal level except occasionally. Usually the contractions were higher than those observed before thyroid was fed, and occasionally high contractions like those observed during the "hyperthyroid" period occurred as long as two months after the thyroid feeding had been stopped.

It is interesting to note that the gastric motility of the dog on which basal metabolism tests were run never reached the normal level during the two months that contractions were recorded following the feeding of thyroid. However, the basal metabolic rate fell from +50 per cent to the normal at the end of the first week after the thyroid feeding was discontinued, and remained there.

2. *The gastro-intestinal activity as observed by the fluoroscopic method.* The progress of the barium meal through the gastro-intestinal tract of the dogs showed a greater uniformity than the contractions of the empty stomach. In four of the dogs the barium meal usually stayed in the stomach until late during the first hour after its ingestion, or during the second hour, when small particles could be observed in the intestines. Food usually reached the ascending colon five hours after feeding. The complete emptying time of the stomach varied between 5 and 10 hours. The colon was not emptied of barium until the next day, about 24 hours

after its ingestion. Two of the dogs showed intestinal rates varying considerably from the above description.

One of these dogs showed a faster normal rate. Barium was always observed in the small intestine within the first hour after feeding. It always reached the ascending colon between the third and fourth hours after feeding. The emptying time of the stomach was variable, occurring between 6 and 10 hours after feeding. The time of defecation was also variable, barium frequently being given off 2 or 3 hours after it had reached the descending colon. The bulk of the material was not expelled until the following day, however.

One dog showed extremely slow progress of the food through the digestive tract. In only one instance out of four observations was barium observed in the small intestine during the first hour after ingestion. It did not reach the ascending colon until 5 or 6 hours later. The stomach normally showed the presence of barium in small amounts 10 to 11 hours after feeding. In one instance only the stomach was completely empty 8 hours after feeding.

It is interesting to note that the dog whose intestinal rate was abnormally fast was one of those animals showing high gastric motility as revealed by the gastric hunger contractions; and that the dog whose intestinal rate was slower than the others showed low gastric hunger contractions during the period previous to thyroid feeding.

During the period of thyroid feeding increased gastro-intestinal motility was shown by means of the fluoroscope in five of the six dogs. Appreciable quantities of barium always appeared in the intestine during the first hour after its ingestion. Barium appeared in the ascending colon 1 to 2 hours earlier than in the normal condition, or 3 to 4 hours after ingestion. While the emptying time of the stomach appeared to be variable according to the method of observation, the stomach was always emptied at least by the shortest time limit observed in the normal condition. In all except one dog, barium remained in the colon for 24 hours after feeding, as before. In the exceptional dog, the bulk of the barium was always in the descending colon in 8 hours and defecation occurred at the tenth hour in five out of six observations. The stools of this dog were always very soft or fluid in consistency during the period of "hyperthyroidism." In two other dogs the stools were softer in consistency than normal during the "hyperthyroid" period, but nevertheless the barium was retained the normal length of time in the colon.

The dog whose intestinal rate has been described as unusually rapid normally showed no appreciable change during the period of induced hyperthyroidism. However, in this dog, the activity of the empty stomach was increased as recorded by the balloon method.

The intestinal rates of the five dogs which increased during the "hyper-

thyroid" period returned to the previous normal level within two weeks after the thyroid feeding was discontinued.

Discussion. Perussé and Rozen (4) report an increase in the height of gastric contractions in dogs fed daily 2.5 grams desiccated thyroid per kilo body weight. When the dose is increased to 5 grams per kilo body weight they note a preliminary period of depression followed by an increase in height of the gastric contractions. With a 15 gram dosage they report no constant increase in hunger contractions.

Kratinoff (5) reports in four of the six dogs in which he studied the effect of "hyperthyroidism" on gastric contractions, an increase in the hunger contractions during the period of thyroid administration, whether the thyroid was given in one single large dose, or fed daily in small amounts, or whether thyroxine was injected. In two of the six dogs, he reports a depression of the hunger contractions under similar conditions.

All of our six dogs showed an increase in hunger contractions during thyroid feeding, but the effect of administering thyroid in varying doses was not studied. The dose used (0.4 gram per kilo body weight) brought on symptoms similar to those seen in the spontaneous hyperthyroidism of man, including an increase in the basal metabolic rate. Increased gastric motor activity was observed to accompany this condition in our animals.

Kratinoff reports that ten months after daily feeding with 1 gram of desiccated thyroid for a period of thirty days, the gastric contractions were often as high as during the "hyperthyroid" period. He finds that the stomach behaved erratically after "hyperthyroidism," at one time showing a depression in motility, and at another time very high contractions. He concludes that the thyroid has a long continued effect on gastric motility, which he did not explain.

We found a decrease in the activity after the thyroid was discontinued, but we occasionally observed the type of contractions, characteristic of the "hyperthyroid" condition. After two months, the gastric activity had returned to the normal level in only two dogs. The explanation of this long continued action of the thyroid on the stomach is difficult. All other hyperthyroid symptoms disappeared. The dogs gained weight, frequently above the normal level. The nervousness, the elevated body temperature decreased, the polydipsia, and polyurea disappeared; and in the dog on whom basal metabolic studies were made, the basal returned to the normal. We cannot assume therefore that any abnormal amount of functioning thyroid material remains incorporated in the protoplasm long after the thyroid intake is stopped. Careful studies on the blood chemistry of dogs, the effect of low protein and cholesterol values on the gastric contractions, and a study of these values in the blood of dogs long after periods of thyroid feeding might throw some light on these conditions.

Not only is the digestive tract shown to be more active during the time of thyroid feeding by the gastric contractions but also by the barium meal. Inasmuch as diarrhea is a frequent symptom of hyperthyroidism in man, one might expect to find that the barium residue would go through the colon at a greater rate of speed than the normal, so that water absorption would be prevented. This expected condition was actually observed in only one of the six dogs studied. In this dog the stools were definitely of more fluid consistency than the normal. In two other dogs softer stools than normal were observed, but in these dogs the barium residue was retained the usual length of time. In the three other dogs the barium remained in the colon the normal length of time and no symptoms of diarrhea were manifested.

In all dogs except one, however, an increased speed of the barium meal through the stomach and small intestine was noted.

Why the increase in speed of the barium meal should occur in the upper part of the digestive tract is difficult to explain. If the thyroid should act by means of the vagus nerve this effect would be expected, but later studies indicate that the thyroid does not act in this manner. Furthermore, the fact that gastric acidity is decreased rather than increased during hyperthyroidism (17), (18), (19) does not indicate over activity of the vagus. McCann (20) has lately investigated the factors which might influence the emptying time of the stomach. He finds that free hydrochloric acid or the products of digestion have no effect on the emptying time. He finds in the first phase of digestion a limited emptying of the stomach accompanied by great tonic and peristaltic activity of the antrum. As the antrum relaxes in the later phases of digestion, the emptying time decreases. McCann thinks that the activity of the antrum depends on the irritability and stimulating action of raw protein to vigorous tonic and peristaltic contractions. He also thinks that the change of the meal to the more fluid state is a factor influencing the emptying time of the stomach. Should one assume then that the thyroid acts by directly stimulating the muscle to greater activity, one might conclude that one should find delayed emptying of the stomach since the higher activity of the antrum tends to keep food within it, according to McCann. However, the contrary is true. Greater activity of the muscles of the intestinal tract would bring about an increased rate of speed with which barium entered the large intestine, and would therefore explain that finding.

Explanation of the increased intestinal activity might lie in the change in gastric secretion. Since gastric acidity is lessened in hyperthyroidism, protein food is probably not as well digested as in the normal dog, and larger pieces of undigested food might pass into the small intestine acting as a stimulus to peristaltic activity.

SUMMARY

1. Daily feeding of 0.4 gram per kilo body weight of desiccated thyroid per dog increases the activity of the empty stomach of dogs as shown by the type and height of the contractions of the empty stomach. After the thyroid feeding is discontinued there is a lowering of gastric activity, although in two months a return to the normal level was not observed in two dogs.

2. During the period of thyroid feeding the emptying time of the stomach is decreased, and a barium meal passes more rapidly through the small intestine. After the administration of thyroid is stopped, the speed of the barium meal through the digestive tract returns to its former rate.

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